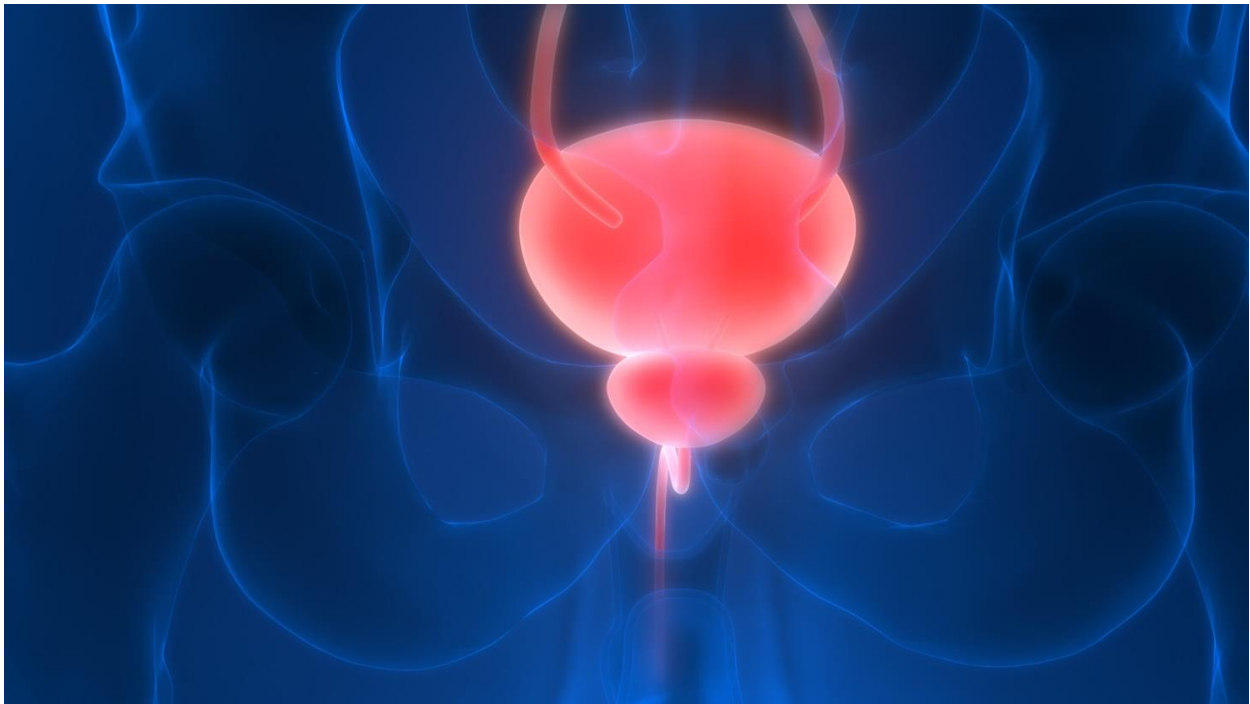


EVIDENCE BRIEF

Duration of Antibiotic Treatment for Uncomplicated Urinary Tract Infection in Long-Term Care Residents



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Key Messages

- Recent evidence suggests that short courses of antibiotics (7 days or less) are appropriate for older adults with uncomplicated lower urinary tract infections.
- There are several advantages to short course antibiotic therapy when compared to longer durations, including less side effects,^{1,2} less risk of antibiotic-resistant organisms^{3,4} and less risk of *C. difficile* infection.⁵

Issue and Research Question

Overuse of antimicrobial therapy in the long term care (LTC) setting is common and leads to patient harm.⁶ Seventy eight (78) % of Ontario LTC residents will receive at least one course of antimicrobial therapy over the course of a year. Of these prescriptions, one third are prescribed for urinary indications. At least one-third of these prescriptions are for asymptomatic bacteriuria, a condition that does not benefit from antimicrobial treatment in older adults.⁷

Sixty three (63) % of prescribed courses of antibiotic treatment in LTC are longer than 10 days. Duration of therapy varies drastically based on prescriber, but not patient characteristics.⁸ This overall long duration and prescriber variability persists when examining management of urinary tract infections. This data suggests that habit and experience play a large role in antibiotic prescribing patterns in long-term care, particularly for urinary tract infections.

Due to the increased susceptibility to UTIs in older individuals, a function of reduced immune response and altered bladder function, elderly are often treated with longer antibiotic courses than younger patients.⁹ However, there is a lack of data that support the concept that longer courses are superior in this population. Additionally, older individuals are more prone to adverse drug events, drug interactions and the collateral damage of antimicrobial resistance.

Uncertainty exists regarding the appropriate management of symptomatic urinary tract infections in residents of LTC homes, particularly with respect to the appropriate duration of therapy. Additionally, there is controversy in North American guidelines with respect to the appropriate duration of treatment for these infections. This document will summarize the literature pertaining to treatment of uncomplicated lower UTI in LTC residents, with a focus on optimal duration of therapy.

Methods

An initial Cochrane Database search was performed to determine if there were any relevant systematic reviews. Following this, a full primary literature search was performed. On November 8, 2016, Public Health Ontario (PHO) Library Services performed a literature search of articles published since 2008 using three databases (MEDLINE, Embase, CINAHL). The search included the concepts “urinary tract infection,” “elderly,” “antibiotic” and “duration.” Both primary literature and review articles were searched to comprehensively capture all relevant literature. English-language articles retrieved by the searches were assessed for eligibility by PHO staff. Articles were included if they were interventional studies comparing short course (<7 days) to longer courses (≥ 7 days) for treatment of uncomplicated lower UTI in elderly individuals. Single-dose studies were excluded.

Main Findings

A Cochrane database search on the topic of “urinary tract infection” revealed 35 reviews, with one relevant to this question. The initial literature search for articles published between May 6, 2008 and November 8, 2016 retrieved 2,236 references. After title and abstract screening, no eligible studies were found on this topic.

A 2008 Cochrane Review (includes all primary literature up until May 6, 2008) examined 15 studies including 1,644 elderly women comparing duration of antibiotic treatment for uncomplicated urinary tract infection (UTI).¹⁰ The authors found that single dose antibiotic therapy was inferior to short or long courses of treatment.

Short course antibiotic therapy (less than 7 days) results in similar outcomes compared to long durations (7-10 days) for cystitis.

However, short course antibiotic therapy (3-6 days) had similar efficacy to long durations (7-14 days).¹⁰ Examining the pooled data, no differences were found in terms of clinical failure with short vs. long treatment (risk ratio: 0.98, 95% confidence interval; 0.62 to 1.54), microbiological persistence (risk ratio: 0.85, 95% confidence interval; 0.54 to 1.32) or discontinuation due to adverse events (risk ratio: 0.11, 95% confidence interval; 0.01 to 1.97). However, one study found a higher risk of adverse effects in elderly that received 7 days compared to a 3 day course of treatment.¹¹

Appendix A includes a table summarizing all studies comparing short course (3-6 days) to long course (7-14 days) of antibiotics for treatment of uncomplicated urinary tract infections in older patients.^{11,21-25}

Discussion and Conclusions

There is a lack of data examining the optimal duration of antibiotic treatment for uncomplicated lower UTI in LTC residents. However, there are several studies in older adults, summarized in a Cochrane review,¹⁰ showing that shorter courses of antibiotics (3-6 days) have similar efficacy to longer courses (7-14 days).

Limitations of this data include:

- Most data is from sub-populations of older adults, resulting in wide confidence intervals, with low precision.
- Majority of RCTs are not designed as non-inferiority analyses and may be underpowered.
- The bulk of studies focus on fluoroquinolones for short course therapy, agents that are no longer considered first line.

Although the Vogel study¹¹ examines the use of fluoroquinolones, it overcomes most of the above limitations. It includes only women over the age of 65 and a subset of hospitalized patients (23%). The study design is a non-inferiority analysis and is adequately powered. Based on this study, it is reasonable to recommend short courses of antibiotics for older residents of LTC homes, particularly when using fluoroquinolones.

A Cochrane review comparing 3 days to 5-10 days of therapy for uncomplicated lower UTI in those aged 18-65 found similar results. Pooled data from 32 trials (9,605 patients) showed no difference in symptomatic failure between short and long course therapy for both short-term (RR 1.06, 95% CI 0.88

to 1.28) and long-term (RR 1.09, 95% CI 0.94 to 1.27) follow-up. Although the longer treatment course was associated with a lower risk of bacteriological failure, the clinical significance of this finding is not clear. No differences were found when looking at subgroups of antibiotic classes (quinolones, sulfonamides, beta-lactams).¹

However, the use of short course beta-lactam treatment in UTI is controversial. A RCT published after this analysis indicated that 3 days of beta-lactam (amoxicillin-clavulanate) therapy was inferior to 3 days of ciprofloxacin.¹² This is in keeping with an older review showing that 5 days of beta-lactam therapy is superior to 3 days of therapy.¹³ This concern is echoed by the Infectious Diseases Society of America (IDSA) Urinary Tract Infection Guidelines that highlight that beta-lactam agents have inferior efficacy compared to other first-line agents and may require a course of 5-7 days to improve efficacy.¹⁴

Neither the Cochrane review in younger nor older patients examined short course nitrofurantoin for uncomplicated UTI; however, there is robust data to support a duration as short as 5 days of nitrofurantoin in these patients.¹⁵

In addition, there are several risks to prolonged courses of antimicrobial therapy. Due to physiological changes associated with aging, older adults are more susceptible to the negative consequences of antibiotics, including adverse effects^{13,16} and drug interactions.²¹ The Cochrane review in patients aged 18-65 with UTI also found an increased risk of adverse effects (gastrointestinal, dermatological) in those with prolonged therapy compared to the shorter duration group. Prolonged antimicrobial therapy has been shown in many studies to result in a greater risk of acquiring antibiotic resistant organisms.^{5,6} Additionally, longer durations of antimicrobial therapy are associated with increased risk of *C. difficile* infection (CDI).⁷ Older adults are already more susceptible to CDI and more likely to suffer morbidity and mortality from this infection.¹⁷

While this review focused on uncomplicated cystitis, there is evidence that shorter courses (7 days) are adequate in men with non-prostatic lower UTI and those with catheter-associated UTIs.¹⁸⁻²⁰ On the other hand, prolonged courses (10-14 days) are still recommended in residents with pyelonephritis, bacteremia or deep-seated infection (e.g., peri-nephric abscess). Even in these scenarios there is emerging evidence that 7 days of treatment might be sufficient.^{26,27}

Given the lack of proven efficacy with longer courses, in combination with the risks associated with prolonged antibiotic therapy, short course treatment (7 days or less) should be used whenever possible for management of uncomplicated UTI in LTC home residents.

Treatment of asymptomatic bacteriuria in LTC residents is not recommended, as it does not improve outcomes and can lead to harm. For more information on preventing treatment of asymptomatic bacteriuria, see Public Health Ontario's [UTI Program](#).

Appendix A

Studies comparing duration of antibiotic therapy for uncomplicated cystitis in older patients

Study	Design	Patients	Intervention	Comparator	Outcomes
Vogel, 2004 ¹¹	Randomized (Non-inferiority, margin=10%) Double blind Multi-center	Uncomplicated lower UTI in women ≥ 65 , hospitalized or ambulatory n=183	Ciprofloxacin 250 mg PO bid x 3 days	Ciprofloxacin 250 mg PO bid x 7 days	Bacterial Eradication: (after therapy) 3 days: 98% 7 days: 93% RR=1.05 (0.93-1.07) Clinical failure (after therapy) 3 days: 0% 7 days: 3% RR=0.36 (0.02-8.63)
Guibert J, 1997 ²¹ (French)	Randomized Open Label Multi-center	Recurrent uncomplicated lower UTI in ambulatory women ≥ 18 years n=421 Subgroup ≥ 50 years n=92	Lomefloxacin 400 mg PO daily x 3 days	Norfloxacin 500 mg PO bid x 10 days	Patient acceptability (little or not satisfied with treatment) 3 days: 4% 10 days: 12% RR 0.35 (0.07-1.72)
Piipo T, 1990 ²²	Randomized Double blind Multi-center	Uncomplicated lower UTI in ambulatory women 18-80 years n=400 Subgroup ≥ 65 years n=65	Norfloxacin 400 mg PO bid x 3 days	Norfloxacin 400 mg PO bid x 7 days	Microbiological failure: 3 days: 17% 7 days: 7% RR= 2.57 (0.56-11.81)
Raz R, 1996 ²³	Randomized Open Label	Uncomplicated lower UTI in ambulatory	Ofloxacin 200 mg PO daily x 3 days	Cephalexin 500 mg PO bid x 7 days	Microbiological failure (after therapy)

Study	Design	Patients	Intervention	Comparator	Outcomes
	Single-center	post-menopausal women n=223			3 days: 23% 7 days: 37% RR= 0.62 (0.41 - 0.94) Clinical failure (after therapy) 3 days: 23% 7 days: 23% RR = 0.98 (0.61 - 1.59) Symptom recurrence (at 28 days) 3 days: 24% 7 days: 33% RR = 0.75 (0.49 -1.13)
Stein, 1992 ²⁴	Randomized Double Blind Multi-center	Uncomplicated lower UTI in women ≥ 18 years n=404 Subgroup ≥65 years n=81	Temafloxacin 400 mg PO daily x 3 days	Ciprofloxacin 250 mg PO bid x 7 days	Clinical failure (after therapy) Nil in both groups
van Merode, 2005 ²⁵	Randomized Single blind Multi-center	Uncomplicated lower UTI in women 13-77 n=129 Subgroup ≥60 years n=26	Trimethoprim PO x 3 days (dose not specified)	Trimethoprim PO x 5 days (dose not specified)	Microbiological failure (after therapy) 3 days: 58% 5 days: 21% RR=2.72 (0.9-8.27) Clinical failure (after therapy) 3 days: 25% 5 days: 21% RR=1.17 (0.29-4.74)

Specifications and Limitations of Evidence Brief

The purpose of this Evidence Brief is to investigate a research question in a timely manner to help inform decision making. The Evidence Brief presents key findings, based on a systematic search of the best available evidence near the time of publication, as well as systematic screening and extraction of the data from that evidence. It does not report the same level of detail as a full systematic review. Every attempt has been made to incorporate the highest level of evidence on the topic. There may be relevant individual studies that are not included; however, it is important to consider at the time of use of this brief whether individual studies would alter the conclusions drawn from the document.

Additional Resources

- [Duration of Antibiotic Treatment for Pneumonia in Long-Term Care Residents](#) (Evidence Brief)
- [Shorter is Smarter: Reducing Duration of Antibiotic Treatment for Common Infections in Long-Term Care](#) (Fact Sheet)
- [Shorter is Smarter: Reduce Duration of Antibiotic Therapy in Long-Term Care](#) (Infographic)
- [Duration of Antibiotic Treatment for Uncomplicated Urinary Tract Infection in Long-Term Care Residents](#) (Evidence Brief)
- [Duration of Antibiotic Treatment for Uncomplicated Cellulitis in Long-Term Care Residents](#) (Evidence Brief)

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Authors

Bradley Langford, Antimicrobial Stewardship Pharmacist Consultant, Infection Prevention and Control, Public Health Ontario.

Contributors

Rita Ha, Antimicrobial Stewardship Pharmacist Consultant, Infection Prevention and Control, Public Health Ontario.

Nick Daneman, Scientist and Physician, Infection Prevention and Control , Public Health Ontario

Kevin Schwartz, Scientist and Physician, Infection Prevention and Control , Public Health Ontario

Reviewers

Dan Dalton, Pharmacist, Medical Pharmacies Group Ltd.

Carrie Heer, Nurse Practitioner, St. Joseph's Health Centre, Guelph

Justin Lin, Pharmacist, Medical Pharmacies Group Ltd.

Heidi Wittke, Director, Clinical, Medisystems Pharmacy

Louis Kennedy, Hospitalist, Providence Care Hospital, Medical Director, Arbour Heights LTC

Allan Grill, Lead Physician, Markham Family Health Team

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Antimicrobial Stewardship Program, Infection Prevention and Control

Email: ASP@oahpp.ca

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